REMARKS

Claims 1-23, 40-55, 61-63, 65, 67, 68, 73-78, 80-85, and 88-109 were pending. Claims 42-55, 61-63, 65, and 88-92 remain withdrawn as being drawn to a non-elected invention. Claim 6-15, 19, 73-76, 79, 83-84, 93-96, and 103-106 are canceled herein. Claims 1-5, 6, 20-23, 41, 67, 77, 82, 97, and 109 are amended herein. New claims 110-125 are added herein. Support for the amendments are found throughout the specification at, *inter alia*, ¶38, ¶94, ¶98, ¶173, and the original claims, and thus it is believed that no new matter is added. Claims 1-5, 16-18, 20-23, 40-41, 67-68, 77-78, 80-82, 85, 97-102, and 107-125 are pending. No claim is allowed.

Formal Matters

According to the Examiner, claim 104 will be objected to under 37 C.F.R. § 1.75 as being a substantial duplicate of claim 79 should claim 79 be found allowable. Applicants note that claims 79 and 104 have slightly different scopes and thus are not substantially identical. Nonetheless, in an effort to expedite the prosecution of the claims, claim 79 is canceled herewith.

Rejections Under 35 U.S.C. § 112, First Paragraph - Written Description

Claims 107-109 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. According to the examiner, the specification lacks support for the esterase activity being limited to "catalysis of a transesterification reaction", "catalysis of a acidolysis reaction", or for the encoded enzyme being thermostable. Claims 1, 3-23, 40, 41, 67, 68, 73-85, and 93-109 are rejected under 35 U.S.C. § 112, first paragraph for reasons of record. In brief, the examiner asserts that the majority of claims contain no functional limitations. For those that have a functional limitation of esterase activity, the examiner alleges that esterase activity encompasses a highly diverse genus and the single disclosed species is not representative of the entire genus. The examiner also alleges that the claims also lack sufficient structural limitations. Applicants traverse these rejections.

The specification as filed provides adequate written description for claims 107-108. For example, the specification discloses at ¶3:

> A principle example of esterases are the lipases, which are used in the hydrolysis of lipids, acidolysis (replacement of an esterified fatty acid with a free fatty acid) reactions, transesterification (exchange of fatty acids between triglycerides) reactions, and in ester synthesis.

These are not new esterase activities, but are well established esterase activities. Thus, such disclosure is sufficient to demonstrate that the inventors had possession of the claimed compositions at the time of filing and thus provides adequate written description for the cited claims.

Claim 109 is amended herewith to further clarify the thermostable enzymatic activity of the claimed polypeptide. The specification discusses the use of enzymes with activity that function at extreme temperatures. *See, e.g.*, the specification at ¶¶ 59, 98. The claim language now clearly indicates that the claimed polypeptide has esterase activity that functions at these extreme conditions. As the person of skill in the art is aware of the boundaries for temperature in which most enzymes function, Applicants believe the specification provides adequate support for the claimed composition.

Applicants respectfully submit that the esterase activity as currently claims is sufficiently specific to meet the requirements of 35 U.S.C. § 112, first paragraph. Esterase activity is a very specific activity - the hydrolysis or synthesis of an ester. There is no diversity in this most basic chemical reaction. Thus, while the array of activities that can include the hydrolysis of an ester bond is broad, it is a specific chemical reaction recognized in the art and easily assessed using routine methods, as evidenced by the declaration of Dr. Jay Short already of record. Applicants have amended the claims to clarify the specific reaction, rendering the remaining claims superfluous.

Applicants also submit that sufficient structural limitations are provided for the claimed compositions. The specification discloses the full sequence of each nucleic acid claimed and the claimed genera is limited to at least 90% sequence identity that encode a polypeptide with an esterase activity. A person of ordinary skill in the art would recognize the inventors had possession of this genera at the time of filing and have sufficient guidance to make and use the claimed compositions with the guidance provided.

Accordingly, it is believed this basis for rejection may be withdrawn.

Rejections Under 35 U.S.C. § 112, First Paragraph - Enablement

Claims 1, 3-23, 40, 41, 67, 68, 73-85, and 93-109 are rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking reasonable enablement for any polypeptide having at least 50% (or 70%) sequence identity to SEQ ID NO:26 and encoding a polypeptide with an esterase activity, or any polynucleotide comprising at least 30 bases of a sequence having 70% identity to SEQ ID NO:26 and encoding a polypeptide with an esterase activity, or any polynucleotide comprising a fragment of SEQ ID NO:26 or encoding fragments of SEQ ID NO:36, or all fragments or variants thereof, or vectors and host cells comprising said nucleic acids for reasons of record. Briefly, the examiner asserts that the specification is completely silent regarding which amino acids can be substituted, deleted, or inserted in SEQ ID NO:26 to obtain structural homologs of the nucleic acid. The examiner also argues that the specification lacks "any clue" regarding which 30 consecutive base fragments of SEQ ID NO:26 are required to encode proteins with esterase activity or which fragments of a nucleic acid having 70% sequence identity to SEQ ID NO:26 are essential for esterase activity. The examiner maintains that it is not routine in the art to randomly create an infinite number of variants and test them for activity. Applicants traverse these rejections.

Applicants respectfully aver that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, a genus of nucleic acids having 90% sequence identity or more (as well as 50% and 70% sequence identity) to SEQ ID NO:26 and 36, and having esterase activity. The specification discloses the manner and process of making and using the claimed nucleic acids with esterase activity in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *See* MPEP § 2164.04, rev. 2, May 2004, pg 2100-189. Therefore, unless there is a reason to doubt the objective truth of the statements contained within the specification as filed, it fulfills the requirements for reasonable enablement. *See In re Marzocchi* 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). The specification discloses the full sequence of the claimed esterase as well as providing guidance regarding changes to esterase sequences that may be made without altering its enzymatic activity. *See, e.g.*, the specification at ¶54. Applicants also have provided the declaration of Dr. Jay Short, attesting to the state of the art regarding such modifications and its routine nature. Moreover, esterase activity is a single basic and well known chemical reaction. While there are any number of substrates available,

the basic activity is known and disclosed in the specification, rendering a person of skill in the art able to make and use the claimed compositions. In light of the guidance provided regarding the structure and specific genera of the claimed compositions, Applicants submit that the specification provides sufficient enablement to meet the requirements of 35 U.S.C. § 112, first paragraph.

Accordingly, it is believed the bases for rejection may be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 2-5, 19-21, 67, 68, 73-81, 83, 84, 97, 99, 104-105, and 109 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. According to the Examiner, claim 2 is confusing in its recitation of "comprising a sequence comprising SEQ ID NO:26 and sequence complementary thereto". Claims 3-5 are allegedly confusing in the recitation of "hybridizing to a nucleic acid comprising (a) a sequence having at least 70% sequence identity to SEQ ID NO:26 and encoding a polypeptide having an esterase activity and (b) sequences complementary to (a)." Claims 19-21 are allegedly confusing in the recitation "wherein the sequence identity is at least X%" as the reference sequence is not identified. Claims 67, 83, 84, and 97 are allegedly indefinite in the recitation of "at least about 30, 35, 40, 45, 50, 75, 100, 150, or 200 nucleotides in length" Claims 79, 104, and 105 are allegedly confusing in reciting lengths of less than 10-50 bases while the claims from which they depend recite minimum lengths of 30 bases. Claims 73-78 are allegedly indefinite in the recitation of "% sequence identity to the nucleic acid". Claim 99 is allegedly indefinite in the inclusion of "a fosmid" in the Markush group as this is not a known type of vector. Claim 109 is allegedly indefinite because the term "thermostable" is a relative term for which the specification does not provide a standard for ascertaining the requisite degree. Applicants traverse these rejections.

Claims 19, 73-76, 83-84, 79, 104, and 105 are canceled herein, rendering these rejections moot.

Claims 67 and 97 are amended herein to indicate that the claimed sequences are at least 30 nucleotides in length. Applicants note that the deleted recitation of "35, 40, 45, 50, 75, 100, 150, or 200" nucleotides does not omit these sizes of nucleic acid sequence from the scope of the claim

as amended herein, but simply clarifies the scope as the smallest nucleic acid sequence is 30 nucleotides in length with the remaining sequence sizes being claimed in new claims 110-125.

Applicants respectfully submit that "fosmid" is a term of art readily understood by one of ordinary skill in the art at the time of filing. Applicants submit herewith a section from the textbook Current Protocols in Molecular Biology as Exhibit A. In this Exhibit, the meaning of the term "fosmid" is shown to be a cosmid vector with a F factor replicator replacing the ColE1 replicator, permitting the vector to be maintained at low copy number and increased stability in *E. coli*. *See* Exhibit A at 1.5.7. The definition provided herein mirrors the explanation of fosmids provided in the specification itself at, *e.g.*, ¶104. Moreover, this section also cites the same publication previously made of record (*i.e.*, Kim et al., Nucleic Acid Res. 20:1083-85 (1992)) as the first description of fosmids. Applicants believe this demonstrates the state of the art at the time of filing, and thus the term "fosmid" is sufficiently definite. *See* MPEP § 2173.02.

Claim 109 is also amended herein to clarify that the claimed compositions retain enzymatic activity at extreme temperatures and thus are thermostable. Applicants note that enzymes typically have a narrow range of temperature over which they are active. However, a thermostable enzyme is one that operates at extreme temperatures as disclosed in the specification. In view of the amendment and the guidance provided in the specification, the metes and bounds of the scope of the claimed compositions is readily apparent to the skilled artisan, and thus the claim at issue is sufficiently definite.

Claims 2-5, 20-21, and 78 are amended herein to clarify the sequences claimed in view of the remaining comments provided by the Examiner. Applicants appreciate the attention given to these claims by the Examiner.

Accordingly, it is believed this basis for rejection may be withdrawn.

Rejection Under 35 U.S.C. § 102 (b)

Claims 3, 5-15, 67-84, 93-97, 103-105, and 107-109 are rejected under 35 U.S.C. § 102 (b) as allegedly being anticipated by Robertson et al., WO 97/30160 for reasons of record. According to the examiner, one of skill in the art would not have recognized that applicants

considered the claimed genera and subgenera to be their invention. Applicants traverse this rejection.

Applicants respectfully submit that the parent applications, Serial No. 08/602,359, filed February 16, 1996, and Serial No. 09/382,242, filed August 24, 1999 provide adequate support for genera and subgenera as currently claimed. Therefore, WO 97/30160 is not a proper reference under 35 U.S.C. § 102 (b).

Accordingly, it is believed this basis for rejection may be withdrawn.

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 564462000820.

Dated: February 11, 2005

Respectfully submitted,

By _____

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